

same TOF acquisition time of 1 s, the intensities of doubly charged bradykinin (SEQ. ID. NO: 1) and fibrinopeptide-A (SEQ. ID NO: 2) ions in the trapping mode are more than an order of magnitude greater than those in the continuous (no trapping) mode. In the trapping mode, the mass spectrum corresponds to 20 trap releases per 1 s (or a sum of 200 TOF pulses), while in the continuous mode, the mass spectrum is obtained as a sum of 9000 TOF pulses.

[0035] FIGS. 11a-11b present ratios of intensities of two exemplary peptides, doubly charged bradykinin (SEQ. ID. NO: 1), and fibrinopeptide-A (SEQ. ID. NO: 2) ions in the trapping and continuous modes as a function of accumulation time at different analyte concentrations, respectively. As shown in the figures, at a concentration of 10 nM, a ~13-fold to ~20-fold signal enhancement was observed for bradykinin in the trapping mode as compared to that obtained in the continuous mode; actual S/N gain was ~35 due to a 3-fold lower chemical background. Sensitivity in trapping mode is an order of magnitude greater than in continuous mode at low concentrations. Sensitivity improvement in the trapping mode is also related to a greater and more efficient ion desolvation and a resulting reduction of chemical background. When the ion population reaches trap capacity, no further increase in sensitivity is expected in the trapping mode. As the trap capacity is reached, no further improvement in S/N was observed. An increase in accumulation time results in lower duty cycle (and signal) as fewer ion packets are introduced to the TOF-MS per unit time at longer accumulation times. Decline at longer accumulation times is due to the reduction in the instrument duty cycle. Signal-to-Noise (S/N) values and noise levels acquired for the 10 nM mixture of bradykinin (SEQ. ID. NO: 1) and fibrinopeptide-A (SEQ. ID. NO: 2) are listed in the following TABLE:

	Bradykinin 2+		Fibrinopeptide A 2+	
	S/N	Noise (counts)	S/N	Noise (counts)
Continuous	15.4	32.1	49.8	14.3
Trapping *	534.9	11.8	988.8	13.5
Ratio (Trapping/Continuous)	34.6	0.4	19.9	0.9

* Trapping Time = 100 ms
Concentration = 10 nM

[0036] Improvement in the S/N of bradykinin (SEQ. ID. NO: 1) is due to an increase in the measured signal intensity and the reduction in noise level. Most background noise is observed in the low m/z range, so chemical noise reduction was not observed for fibrinopeptide-A (m/z 768.8) (SEQ. ID. NO: 2). Enhancements in (S/N) are attributed to a combination of an increase in the number of transmitted ions to the TOF detector due to ion accumulation, to more efficient desolvation of the analyte ions, and to removal of chemical background peaks following the desolvation of smaller ions in the ion trap.

[0037] The following examples provide a further understanding of the invention in its broader aspects.

Example 1

IFT Characterization Using Ion Mobility, TOF-MS

[0038] Characterization of the IFT was conducted using two modes of detection: (1) IMS-only using a Faraday plate

as a charge collector and (2) a commercial TOF instrument interfaced to a custom-built IMS drift cell.

[0039] ESI Source. The ESI source consisted of a chemically etched, 20- μ m-i.d. emitter [Ref. 30] connected to a transfer capillary (150 μ m, Polymicro Technologies, Phoenix, Ariz.) using a zero dead volume stainless steel union (Valco Instrument Co. Inc., Houston, Tex.). Sample solutions were infused using a syringe pump (Harvard Apparatus, Holliston, Mass.) at a flow rate of 300 nL/min. High voltage used to sustain the electrospray ionization (ESI) source was applied through a stainless steel union by a current-limited four-channel power supply (Ultravolt, Ronkonkoma, N.Y.) and held ~2400 V above the heated capillary inlet (150° C.). The electrospray-generated ion plume was sampled using a 64-mm-long transfer capillary with an inner diameter of 0.43 mm. Potential applied to the heated transfer capillary was 210 V higher than the ion mobility drift tube voltage.

Example 2

Ion Mobility-Quadrupole-Time-of-Flight Mass Spectrometer

[0040] The current ion mobility system was comprised of four units, each of which contained 21 0.5-mm-thick copper drift rings [80 mm outer diameter (o.d.) X 55 mm inner diameter (i.d.)] separated by ~10-mm spacers comprised of polytetrafluoroethylene, also known as TEFLON®, and connected in series with 1-M Ω high-precision resistors. High voltage for the ion mobility drift cell was supplied by the same four-channel power supply used to drive the ESI source. An 80-mm-long conventional ion funnel located at the terminus of the ion mobility drift cell was used to refocus the disperse ion clouds that exited the IMS drift cell. Inner diameters of the ring electrodes (0.5 mm thick separated by 0.5-mm TEFLON® sheets) decreased linearly from 51 mm to 2.5 mm at the conductance limit, which was held at 35 V. Custom-built power supplies were used to apply rf-voltages and dc-voltages across the brass electrodes in the outlet portion of the IFT. Peak-to-peak rf-voltage was 115 V_{p-p} at a frequency of 500 kHz, and the dc-gradient electric field was adjusted to match the electric field within the IMS drift cell. Pressures (2-4 Torr) inside the IFT and ion mobility drift cell were monitored using a capacitance manometer and regulated using a leak valve that passed dry, high-purity nitrogen into the drift chamber. To maintain a buffer gas flow counter to the direction of ion velocity, the pressure in the drift cell was maintained ~30 mTorr higher than the IFT. For IMS experiments using 4 Torr N₂, an electric field of ~16 V/cm was established throughout the IMS drift cell and rear ion funnel. For 2 Torr IMS experiments, the same Townsend number was maintained. Unless stated otherwise, all IMS experiments were conducted at 20±1° C. A shielded Faraday plate was placed immediately following the conductance limit in the outlet portion of the IFT for conducting ion current measurements. Ion signals were amplified using a current amplifier (Keithley Instruments, Inc., Cleveland, Ohio); data were recorded using an oscilloscope (e.g., a TDS-784C oscilloscope, Tektronix, Richardson, Tex.). For experiments employing a TOF mass spectrometer as a detector, a segmented quadrupole consisting of two 11-mm sections following the conductance limit of the rear ion funnel served to optimize ion transmission through a 2.5-mm conductance limit (~15 V). The two sections of the quadrupole were biased to 30 and 22 V, with an rf-potential of 200 V_{p-p} at a frequency